

REMARKS

Claims 1, 3, 6, 8, 10, and 16 have been amended. Support for the amended claims can be found in the original claims and on pages 3, 4, and 5 of the specification. Claims 7, 12-13, 15, and 21-30 have been cancelled without prejudice. Claims 31 and 32 have been added. Support for claims 31 and 32 can be found in the original claims and on pages 3-5 of the specification. No new matter has been added. With entry of this Amendment, claims 1-6, 8-11, 14, 16-20, and 31 will be pending. The Applicant respectfully submits that the newly-presented claims are in condition for allowance.

The declaration was objected to by the Examiner. A new declaration in compliance with 37 C.F.R. 1.67(a) is being submitted herewith.

Claims 1-30 were rejected under 35 U.S.C. § 103(a), as being unpatentable over U.S. Patent No. 6,425,949 ("Lemaitre"). In light of the cancellation of claims 7, 12-13, 15, and 21-30, the rejection to these claims is now moot.

Independent Claim 1 and Dependent Claims 2-6, 8-11, 14, and 16-20

Independent claim 1 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Lemaitre.

Amended independent claim 1 recites: "A self setting calcium phosphate cement comprising: (i) a powdered component selected from the group consisting of calcium phosphate, dicalcium phosphate anhydrous, dicalcium phosphate dihydrate, α -tricalcium phosphate, tetracalcium phosphate, hydroxyapatite, octacalcium phosphate or substituted forms thereof, a carbonate, silicate, nitrate, oxide or sulphate and/or a salt of calcium, zirconium, aluminium, titanium or silicon, or mixtures thereof, said powdered component having an average particle size d_{50} of less than 15 μm , and (ii) a calcium phosphate based powder selected from the group consisting of tetracalcium phosphate, α -tricalcium phosphate, hydroxyapatite, monocalcium phosphate monohydrate, monocalcium phosphate anhydrous or mixtures thereof, said powder having an average particle size d_{50} greater than that of the powdered component, said powdered component and said calcium phosphate based powder being suspended in water containing a dissolved zeta potential increasing additive in an amount of from 0.1 to 2 Mol per litre of water

and in sufficient quantity to increase the zeta potential of the suspended particles to at least -30 mV, and wherein the zeta potential increasing additive is chosen to be compatible with the setting pH of the same calcium phosphate cement without the zeta potential increasing additive.”

Amended claim 1 now recites non-acidic cements. In contrast, Lemaitre relates exclusively to a brushite (or acidic) cement (see col. 1, line 2 and col. 2, lines 6-10). For this reason alone, Lemaitre does not teach or suggest the subject matter of claim 1.

Additionally, the setting rate controllers in Lemaitre, such as sodium acetate and sodium citrate, are not “chosen to be compatible with the setting pH” of the cement, as required by claim 1. The Examiner stated that “both citric acid and the citrate of the reference will release citrate ions, which are responsible for setting rate control.” However, citric acid and citrate will not have the same effect on rate control in the same type of cement. Unexpected results are obtained by choosing a zeta potential increasing additive that is compatible with the setting pH of the cement. In other words, acidic cements make use of an acid additive whereas non-acidic cements make use of a salt of the acid.

For example, the Applicant has demonstrated that there is an unexpected difference between the effects of adding 0.5M citric acid and 0.5M sodium citrate to a non-acidic TTCP/DCPA cement. *See* Figure 1 and Specification, page 11. The sodium citrate containing cement is readily injectable at a low force, while the citric acid containing cement can only be injected to 13%. This is an even poorer result than that achieved with the additive-free cement.

In addition, by selecting a zeta potential increasing additive that is compatible with the setting pH of the cement, compressive strength of a non-acidic cement also increases with increasing concentration of sodium citrate. *See* Table 1. The strength of a non-acidic cement sample containing 500mM sodium citrate is 102.4 MPa relative to 62.5 MPa for a sample made with water alone, or 67.1 MPa for a sample made with 500mM citric acid.

The same type of effect can be seen with acidic cements using citric acid. *See* Table 9. For a given powder to liquid ratio, an increase in citric acid concentration in an acidic cement results in an increase in injectability. An increase in sodium citrate concentration in an acidic cement results in a decrease in injectability.

Finally, the setting rate controllers used in Lemaitre are at a lower concentration than required by claim 1, namely, from 0.1 to 2 Mol per litre. For example, the concentration of sodium pyrophosphate in Example 1 is 0.068 M (molecular weight of sodium pyrophosphate is 222, which results in 0.054 mM in 0.8mL of solution). In Examples 4 and 5, a 0.1M solution of sodium pyrophosphate is used. However, this is further diluted by other components so the concentration of sodium pyrophosphate is less than 0.1 M.

In view of the foregoing, independent claim 1 is allowable. Consideration and allowance of independent claim 1 are respectfully requested.

Claims 2-6, 8-11, 14, and 16-20 ultimately depend from allowable claim 1 and therefore are allowable. In addition, claims 2-6, 8-11, 14, and 16-20 may contain additional patentable subject matter for reasons that may not be discussed herein. Allowance of these claims is respectfully requested.

Independent Claim 31

New claim 31 recites: “A self setting calcium phosphate cement comprising: (i) a powdered component, said powdered component having an average particle size d_{50} of less than 15 μm , and (ii) a calcium phosphate based powder, said powder having an average particle size d_{50} greater than that of the powdered component, said powdered component and said calcium phosphate based powder being suspended in water containing a dissolved zeta potential increasing additive in an amount of from 0.1 to 2 Mol per litre of water and in sufficient quantity to increase the zeta potential of the suspended particles to at least -30 mV, and wherein the zeta potential increasing additive is chosen to be compatible with the setting pH of the same calcium phosphate cement without the zeta potential increasing additive and wherein neither said powdered component nor said calcium phosphate based powder is β -tricalcium phosphate.”

Applicant respectfully submits that new independent claim 31 is allowable over Lemaitre. Claim 31 excludes acidic cements by specifying that “neither said powdered component nor said calcium phosphate based powder is β -tricalcium phosphate.” In contrast, Lemaitre relates exclusively to a brushite (or acidic) cement (see col. 1, line 2 and col. 2, lines 6-10).

Additionally, the setting rate controllers in Lemaitre, such as sodium acetate and sodium citrate, are not “chosen to be compatible with the setting pH” of the cement, as required by claim

31. Unexpected results are obtained by choosing a zeta potential increasing additive that is compatible with the setting pH of the cement. In other words, in claim 31, non-acidic cements make use of a salt of the acid. Lemaitre discusses an acidic cement using a sodium citrate, which is contrary to the subject matter of claim 31. As has been demonstrated above, it would not achieve the same results as the subject matter of claim 31.

Finally, the setting rate controllers used in Lemaitre are at a lower concentration than required by claim 31, namely, from 0.1 to 2 Mol per litre. For example, the concentration of sodium pyrophosphate in Example 1 is 0.068 M (molecular weight of sodium pyrophosphate is 222, which results in 0.054 mM in 0.8mL of solution). In Examples 4 and 5, a 0.1M solution of sodium pyrophosphate is used. However, this is further diluted by other components so the concentration of sodium pyrophosphate is less than 0.1 M.

In view of the foregoing, independent claim 31 is allowable. Consideration and allowance of independent claim 31 are respectfully requested.

Independent Claim 32

New claim 32 recites: “A self setting calcium phosphate cement comprising: (i) a powdered component selected from the group consisting of calcium phosphate, dicalcium phosphate anhydrous, dicalcium phosphate dihydrate, α -tricalcium phosphate, tetracalcium phosphate, hydroxyapatite, octacalcium phosphate or substituted forms thereof, a carbonate, silicate, nitrate, oxide or sulphate and/or a salt of calcium, zirconium, aluminium, titanium or silicon, or mixtures thereof, said powdered component having an average particle size d_{50} of less than 15 μm , and (ii) a calcium phosphate based powder selected from the group consisting of tetracalcium phosphate, α -tricalcium phosphate, hydroxyapatite, monocalcium phosphate monohydrate, monocalcium phosphate anhydrous or mixtures thereof, said powder having an average particle size d_{50} greater than that of the powdered component, said powdered component and said calcium phosphate based powder being suspended in water containing a dissolved zeta potential increasing additive in an amount of from 0.1 to 2 Mol per litre of water and in sufficient quantity to increase the zeta potential of the suspended particles to at least -30 mV, and wherein the zeta potential increasing additive is an oligocarboxylic acid compound selected from the group consisting of a group I or group II metal salt, an ammonium salt or a mixed salt.”

Applicant respectfully submits that new independent claim 32 is allowable over Lemaitre. Claim 32 recites non-acidic cements and zeta potential increasing additives selected from the group consisting of a group I or group II metal salt, an ammonium salt or a mixed salt. In contrast, Lemaitre relates exclusively to a brushite (or acidic) cement (see col. 1, line 2 and col. 2, lines 6-10). The setting rate controllers in Lemaitre include sodium acetate and sodium citrate. In other words, Lemaitre discloses the salt form of setting rate controllers for use with acidic cements, whereas claim 32 recites the salt form of zeta potential increasing additives for use with non-acidic cements. Some of the unexpected results and advantages that are obtained by choosing Applicant's non-acidic zeta potential increasing additive with non-acidic cements are discussed above with respect to claim 1.

Finally, the setting rate controllers used in Lemaitre are at a lower concentration than required by claim 32, namely, from 0.1 to 2 Mol per litre. For example, the concentration of sodium pyrophosphate in Example 1 is 0.068 M (molecular weight of sodium pyrophosphate is 222, which results in 0.054 mM in 0.8mL of solution). In Examples 4 and 5, a 0.1M solution of sodium pyrophosphate is used. However, this is further diluted by other components so the concentration of sodium pyrophosphate is less than 0.1 M.

In view of the foregoing, independent claim 32 is allowable. Consideration and allowance of independent claim 32 are respectfully requested.

CONCLUSION

In view of the foregoing, allowance of the application is respectfully requested. The Examiner is strongly encouraged to contact the undersigned by telephone at the Examiner's convenience should any issues remain.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Gregory J. Hartwig', with a stylized, cursive flourish extending from the end.

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